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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/595,845	05/16/2006	Filippo Giancotti	MSK.P-076	7804

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EXAMINER	
HADDAD, MAHER M	
ART UNIT	PAPER NUMBER
1644	
MAIL DATE	DELIVERY MODE
05/13/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/595,845	GIANCOTTI, FILIPPO	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 15-22* is/are pending in the application.

4a) Of the above claim(s) *6,10,16,18 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5, 7-9, 15, 17, 19 and 21-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 16, 2009 has been entered.

2. Claims 1-10 and 15-22 are pending.

3. Claims 6, 10, 16, 18 and 20 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions.

4. Claims 1-3, 5, 7-9, 15, 17, 19 and 21-22 are under consideration in the instant application as they read on a method for inhibition of angiogenesis in a tissue expressing $\alpha 6\beta 4$ integrin, comprising the steps of exposing the tissue to a therapeutic agent effective to reduce the amount of active $\alpha 6\beta 4$ integrin in the tissue, wherein the therapeutic agent targets $\beta 4$, wherein the therapeutic agent is an antibody.

5. The references listed on the PTO-892 were used in Applicant's remarks and provided on 1/20/09 submission. Accordingly, the references will not be supplied.

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-3, 5, 7-9, 15, 17, 19 and 21-22 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 6, 14-20 and 23-24 of copending Application No. 10/596,364. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications use inhibitors of α6β4 integrin that target β4 as therapeutic agents to inhibit tumorigensis in individuals, including humans, of tumors that express α6β4 integrin, wherein the agent is antibody.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-3, 5, 7-9, 15, 17, 19 21 and 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is not in possession of "agent targets β4" in claims 1 and 7, wherein the agent is antibody in claim 5, 9, 15, 17 and 19. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

Neither the exemplary embodiments nor the specification's general method appears to describe structural features, in structural terms, that are common to the genus. That is, the specification provides neither a representative number of species (agent targets β4) to describe the claimed genus, nor does it provide a description of structural features that are common to species (agent targets β4). The specification provides no structural description of agent targets β4 other than ones specifically exemplified; in essence, the specification simply directs those skilled in the art to go figure out for themselves what the claimed agent targets β4 looks like. The specification's disclosure is inadequate to describe the claimed genus of agent targets β4.

The specification fails to provide anti-β4 antibodies or RNAi that blocks activate signal transduction that can be used in the claimed method.

Applicant has disclosed only anti-β4 antibody; therefore, the skilled artisan cannot envision all the contemplated agent possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant's arguments, filed 3/4/09, have been fully considered, but have not been found convincing.

Applicant submits that numerous antibodies, oligonucleotides and binding proteins have been discussed and disclosed by the specification. These provide some examples of potential agents. A person skilled in the art would be able to look at these agents, as well as the knowledge that the C-terminal region controls signaling function, to determine characteristics of a broad range of agents that would target the known sequence of this region. Given the high level of skill in the art, practitioners would accept that an adequate description of α6β4 integrin would put an inventor in possession of antibodies, antisense oligonucleotides, and other agents that would target β4. Sufficient diverse examples with similar activity, such as antibodies and antisense oligonucleotides, have been provided to support this generic claim with written description.

However, Applicant did not describe the claimed "agent that targets and inhibits the signaling function of β4" sufficiently to show they had possession of the claimed genus of agent. It is the examiner's position that the prior of Sepp et al teachings that inhibiting the signaling function of

β4 does not lead to the inhibition of angiogenesis. Accordingly, it is not clear that the listed human and mouse RNAi species and anti-β4 antibodies would function as claimed. With respect to the two anti-β4 antibodies disclosed in the specification, they have not been show to inhibit β4 integrin signaling. Applicant fails to address the issue with respect to the "agent targets and inhibits the signaling function of β4", the rejection is maintained for reasons of record.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e1) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

35 U.S.C. § 102(e), as revised by the AIPA and H.R. 2215, applies to all qualifying references, except when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. For such patents, the prior art date is determined under 35 U.S.C. § 102(e) as it existed prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. § 102(e)).

11. Claims 1-3, 5, 7-9, 15, 17, 19 and 21-22 are rejected under 35 U.S.C. 102(e)/(b) as being anticipated by US 20030224993 (IDS reference)/WO 02/30465.

The `993/`465 publication teaches and claims methods of inhibiting proliferation of cancer cell selected from the group consisting of melanoma, adenoma, lymphoma, myeloma, carcinoma, plasmocytoma, sarcoma, glioma, thyoma, leukemia, skin cancer, retinal cancer, breast cancer, prostate cancer, colon cancer, esophageal cancer, stomach cancer, pancreas cancer, brain tumors, lung cancer, ovarian cancer, cervical cancer, hepatic cancer, gastrointestinal cancer, and head and neck cancer cells (pathological angiogenesis diseases as evidenced by published claims 125-126) comprises contacting a β4 integrin with a composition that inhibits ligand binding (see published claims 1, 2, 10, 13, 38, 41, 45, 106, 121-126 in particular), such as antisense molecules to beta4 mRNA (see published claims 28-29 in particular). The `993 publication teaches that antibodies can be used as integrin inhibitor (see ¶¶ 47-48 in particular).

The reference teachings anticipate the claimed invention.

Applicant's arguments, filed 3/4/09, have been fully considered, but have not been found convincing.

Applicant submits that Land does not teach all of the elements of the claimed invention. As the Examiner previously stated, the binding/adhesion function of β4 is quite separate from the

signaling function, both spatially and temporally. Land merely teaches targeting of the binding portion, while teaching nothing about the signaling portion. This is the focus of the current invention, and land teaches nothing about this.

However, it is the Examiner's position that the prior art antibody would inhibit the signaling function of β4 integrin in the absence of evidence to the contrary. Applicant cannot represent to the public that their claimed antibody can be functionally blocking antibody such as anti-beta4 mAb ASC-3 or 346-11A taught by the prior art (see ¶39 of the instant specification), while at the same time discounting the relevance of that anti-beta-4 antibody to the anticipation of their claims. The teachings of the specification appear to be commensurate with Land publications. If the specification is enabling, so too is the references, and the claims may be unpatentable over the teachings of the reference. If the reference is not enabling, neither is the specification, and the claims may again be unpatentable. The burden is thus placed on Applicant to point out how the teachings of the specification go beyond those of the prior art in identifying therapeutic antibodies.

Applicant submits that Land teaches nothing about inhibiting angiogenesis. In the case of a method claim, a showing of anticipation requires that practicing the method described in the art would inherently (i.e. necessarily) achieve the undisclosed result which it the object of the claimed method, i.e. inhibiting angiogenesis. Exparte Levy, 17 USPQ2d 1461, 1464 (BPAI 1990)(To establish anticipation under the theory of inherency, "the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art."). Land teaches inhibition of proliferation. The Examiner has given no evidence that targeting the β4 binding region would inherently result in inhibition of angiogenesis. As stated above, the two region have very different functions and locations.

However, the claims are drawn to the "inhibition of pathological angiogenesis in a tissue prone to pathological angiogenesis and expressing α6β4 integrin." All the cancer condition taught by the prior art of Land are prone to pathological angiogenesis and expressing α6β4 integrin as evidence by published claims 2, 3 and 5 that the reference cancer cell express α6β4 and that these integrins are suspected to play a role in invasion and metastasis (pathological angiogenesis) (see ¶359 of Land). Further, as evidenced by the specification on ¶67 that melanoma cells, lung carcinoma cells and lymphoma cells are tissue prone to pathological angiogenesis and expressing α6β4 integrin. Again, Applicant cannot represent to the public that their claimed pathological angiogenesis conditions can be melanoma cells, lung carcinoma cells and lymphoma cells (see ¶67 of the instant specification), while at the same time discounting the relevance of that these pathological angiogenesis conditions to the anticipation of their claims.

Applicant further argues that particular antibodies are not disclosed in the prior art references. While the cited paragraphs generally state that antibodies may be used to inhibit function, no specific targets are given. There is no sequence or structure given for the antibodies, nor is a target given. In addition, even if a target were given, the antibody would not necessarily be

functional to inhibit the signaling function of β4 as the only region discussed in the reference is the binding region of β4.

However, it appears that applicant is arguing limitations that are not claimed. There is no specific antibody recited in the claimed invention. The claims are drawn generically to any antibody that would target and inhibit the signaling function of β4. However, the mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Even though applicant has proposed or claimed the mechanism by which anti-β4 antibodies inhibit pathological angiogenesis of tumor does not appear to distinguish the prior art teaching the same methods to achieve the same end-results. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

12. Claims 1-3, 5, 7-9, 15, 17, 19, 21-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Abdel-Ghany et al (JBC, 276(27):25438-25446, 2001) (IDS reference).

Abdel-Ghany et al teach a method of treating breast cancer in mice comprising administering an antibody that binds β4, wherein the breast cancer expresses α6β4. Abdel-Ghany et al teach that adhesion is augmented by an increased surface expression of the α6β4 integrin in breast cancer cells selected in vivo for enhanced lung colonization but abolished by the specific cleavage of the β4 integrin with matrilysin (agent targets and inhibits the signaling function of β4). Abedel-Ghany et al teach that β4 integrin blocking antibodies directed against β4 inhibit lung colonization, while overexpression of the β4 integrin in a model murine tumor cell line of modest lung colonization potential significantly increases the lung metastatic performance. The mice had human breast cancer cells MDA-MB-231 (see abstract and page 25442, 2nd¶, under *Lung Metastasis is Inhibited by β4/hCLCA2 adhesion-blocking Antibodies*).

The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Even though applicant has proposed or claimed the mechanism by which anti-β4 antibodies inhibit pathological angiogenesis of tumor does not appear to distinguish the prior art teaching the same methods to achieve the same end-results. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. *In re Wiseman*, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. *In re Baxter Travenol Labs*, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

The reference teachings anticipate the claimed invention.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

May 7, 2009

/Maher M. Haddad/
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